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Analysis of Differential Gene Expression in *C. elegans* Expressing TDP-43 Shows Evidence of Glutamate Excitotoxicity

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Analysis of Differential Gene Expression in *C. elegans* Expressing TDP-43 shows evidence of Glutamate Excitotoxicity

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Neurons use neurotransmitters as signaling molecules to communicate with other neurons. These chemical molecules can be excitatory, inhibitory, or modulatory. Excitatory neurotransmitters, such as glutamate and acetylcholine, can trigger an action potential, an electrical event that is generated in the axon. Action potentials allow the release of neurotransmitters into the synaptic cleft, the junction between the axon of one neuron and the dendrites of another. Inhibitory and modulatory neurotransmitters maintain balance between neuronal communication and prevents hyperstimulation. Neurotransmitters are necessary for proper neuronal function but lead to toxicity if unregulated. For instance, glutamate is an excitatory neurotransmitter and can cause neuronal damage via excitotoxicity. *C. elegans* and *H. sapiens* have a conserved transfer of neuronal information; sensory neurons to interneurons to motor neurons, as well as share 7 neurotransmitters. Based on these fundamental similarities, we are using *C. elegans* to examine the toxic effects of TDP-43. TDP-43 is an RNA binding protein that aggregates in neurodegenerative disorders, such as amyotrophic lateral sclerosis, a fatal progressive disease that primarily affects motor neurons. Disruptions in neuronal transmissions in TDP-43 transgenic *C. elegans* may provide insight into its many behavioral deficits. Deep sequencing analysis of mRNA ribosomal fragments revealed gene expression changes between transgenic animals and wildtype. Of the 264 upregulated and 20 down regulated genes we analyzed, 32% of upregulated and 32% of downregulated genes were associated with glutamatergic neurons. Therefore, we conclude that excitotoxicity in the mechanosensory and chemosensory pathways likely contribute to the defects in TDP-43 expressing *C. elegans*.